Exhibit 3

The Value Of Antihypertensive Drugs: A Perspective On Medical Innovation

Why don't Americans do better at controlling hypertension, if the societal return on investment is so high?

by David M. Cutler, Genia Long, Ernst R. Berndt, Jimmy Royer, Andrée-Anne Fournier, Alicia Sasser, and Pierre Cremieux

ABSTRACT: Using national survey data and risk equations from the Framingham Heart Study, we quantify the impact of antihypertensive therapy changes on blood pressures and the number and cost of heart attacks, strokes, and deaths. Antihypertensive therapy has had a major impact on health. Without it, 1999–2000 average blood pressures (at age 40+) would have been 10–13 percent higher, and 86,000 excess premature deaths from cardiovascular disease would have occurred in 2001. Treatment has generated a benefit-to-cost ratio of at least 6:1, but much more can be achieved. More effective use of antihypertensive medication would have an impact on mortality akin to eliminating all deaths from medical errors or accidents. [*Health Affairs* 26, no. 1 (2007): 97–110; 10.1377/hlthaff.26.1.97]

MANY ANALYSTS AGREE THAT MEDICAL INNOVATION, whether in the form of new drugs, medical devices, diagnostic techniques, or procedures, has resulted in substantial improvements in both quality and length of life. However, estimating the actual societal value of medical innovation remains a challenge. The medical literature reports results from scores of randomized clinical trials measuring the relative safety and efficacy of specific treatments on individuals in highly controlled settings, but there are few careful estimates of the societal impact of specific medical innovations with real-world average rates of diagnosis, compliance, and clinical impact.

Real-world experience may differ from that in highly controlled clinical trials. Patient compliance rates may be lower. Further, the overall population may be

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"Innovation that results in more benefits than costs is socially beneficial, whether or not it increases spending."

more heterogeneous and may not experience the same level of clinical effect observed with carefully selected populations. In addition, other factors affecting rates of disease, such as demographic factors or health habits, may differ or may change over time. Finally, the potential impacts of medical innovation vary widely. Some innovations greatly improve the quality or length of life, but at a high cost; others result in less substantial improvements, but at a lower cost. Previous research has also distinguished between innovations that result in "treatment substitution," where a new technology replaces an older, likely less effective but also less expensive one, and "treatment expansion," where a new technology results in an increase in the population treated.[1] Innovation that results in more benefits than costs is socially beneficial, whether or not it increases spending.

Comparison of benefits and costs is most appropriately measured at the disease level, thereby isolating the contribution of new technology to improvements in health from other factors. Earlier research has examined such diverse examples as the value of treatment for heart attacks, cataracts, low-birthweight infants, breast cancer, and depression.[2] In this paper we examine the management of chronic high blood pressure through antihypertensive drug therapy, to estimate its impact on the U.S. population over the past four decades and potential further improvements if recommended guideline blood pressure control were achieved for all. We use the hypothetical absence of therapeutic innovation to control blood pressure during that time span to estimate improvements in life expectancy attributable to improved blood pressure control. By assigning a monetary value to these improvements, we estimated a benefit-to-cost ratio for antihypertensive therapy. We also estimated maximum additional health improvements in a hypothetical world of full compliance with blood pressure guidelines.

The Case Of Hypertension

■ **Importance of high blood pressure control.** Hypertension is a risk factor for conditions including coronary heart disease (CHD), myocardial infarction (MI), and stroke. More than fifty million adults were hypertensive in 1999–2000, including 43 percent of adults age forty and older (that is, had Stage I or II blood pressures or reported taking antihypertensive medicine).[3] The risk of developing hypertension increases with age; lifetime risk is estimated at approximately 90 percent for people with normal blood pressures at age fifty-five or sixty-five and who survive to age eighty to eighty-five, respectively.[4] The economic burden of CHD and stroke is substantial. Applying the previous methodologies of Dorothy Rice and colleagues and of Thomas Hodgson and Alan Cohen to 2002 data, we calculate the total economic burden of CHD and stroke at $120.6 billion and $48.9 billion, respectively.[5]

The public health importance of improved management of high blood pressure and of the care and prevention of cardiovascular disease (CVD, the leading U.S. cause of death) is substantial. As Franklin Roosevelt's cardiologist observed, "I have often wondered what turn the subsequent course of human history might have taken if the modern methods for the control of hypertension had been available."[6] On a societal rather than individual level, improvements in CVD mortality have been one of the most important public health successes of the past century. Since 1950, CVD mortality has declined by over half, contributing more than any other factor to life expectancy increases experienced in the past few decades.

■ **Improvements in hypertension treatment.** Drug therapy for hypertension has improved greatly over the past four decades. Limited drug therapy was in use in the 1950s and early 1960s; the only drug therapies for hypertension approved by the Food and Drug Administration (FDA) by 1955 were vasodilators (approved in 1946) and peripherally acting agents (1953).[7] Most patients who today would be treated immediately with effective drug therapy were untreated or treated less effectively. Even knowledge of whom to treat was limited. For example, although *Harrison's Principles of Internal Medicine* (1962) found that diastolic blood pressure was important in determining mortality, it justified treatment only in properly selected cases, stating: "A woman who has tolerated her diastolic pressure of 120 for 10 years without symptoms or deterioration does not need specific treatment for hypertension."[8] Even as late as 1971–75, only 9 percent of the population age forty and older with hypertension reported taking antihypertensive medication, and blood pressures were poorly controlled; 79 percent of this treated group still had Stage I or II blood pressures. Thus, the earlier 1950s–early 1960s time period could be called "drug-naïve" with regard to widespread use of a range of effective drug therapies.

Over time, additional antihypertensive drugs became available: oral diuretics (late 1950s and early 1960s), calcium channel blockers and beta-blockers (1970s and 1980s), and angiotensin-converting enzyme (ACE) inhibitors and angiotensin-receptor antagonists (1980s and 1990s). In addition, knowledge about when to treat hypertension improved. Landmark studies in the late 1960s and early 1970s showed that treating asymptomatic hypertension reduced mortality. We calculate, using data from the National Health and Nutrition Examination Survey (NHANES), that in 1999–2000, 61 percent of the population age forty and older with hypertension reported taking antihypertensive medication.

What has the improved treatment of high blood pressure contributed to U.S. public health? Without these improvements in treatment and prevention, what would cardiovascular morbidity and mortality have been, controlling for changes in risk factors such as smoking, obesity, and population age? Despite documented major strides in CVD management, there has been little systematic examination of the total impact of antihypertensive therapy on health outcomes.

The Approach

The impact of antihypertensive therapy can be measured using results of clinical trials. However, such an approach would reflect treatment effects in selected populations under well-controlled conditions likely to differ greatly from actual clinical practice because of less-than-full compliance, differences in population characteristics, and variations in treatment patterns. To capture the real-world effect of antihypertensives, we used a three-step process based on publicly available data that reflect actual patient treatments and outcomes in the general population. Our approach compared average blood pressures observed in 1999–2000 with those we predicted would have been experienced without antihypertensive drugs. After controlling for all available quantifiable factors, we calculated the impact of antihypertensive therapy as the difference between the two blood pressures that is unexplained by other measurable factors. This methodology does not prejudge the potential effect of therapy on blood pressure and could result in a negative, positive, or null effect.

Our three-step process was as follows. First, we used national survey data to estimate blood pressures (BPs) in the absence of antihypertensive therapy and compared them with BPs actually observed in 1999–2000, to infer the impact of antihypertensive medication on BPs. Second, we used risk equations from the Framingham Heart Study to estimate the impact of lowered BPs on the risk and number of MIs and strokes (2002) and deaths (2001). Third, we assigned a monetary value from the literature to the medication-related improvement in overall life expectancy, and we compared it to average spending on antihypertensives.

■ **Predicting blood pressure in the absence of antihypertensive therapy.** To estimate the impact of antihypertensive therapy on BPs, data from the 1959–62 National Health Examination Survey (NHES) and 1999–2000 NHANES were used. In each case, all respondents were included (5,046 people ages 30–79 in 1959–62; 2,284 people ages 40–79 in 1999–2000). We used the earlier data to estimate a BP prediction equation in the absence of effective medication. Determinants of hypertension, including body mass index (BMI), diabetes, family history, excessive alcohol use, high-salt diet, lack of exercise, race, age, and sex were identified from literature searches. Our final model included BMI, BMI^2 (to account for possible nonlinearities in the effect of BMI on BP), diabetes (yes/no, based on whether the person reported taking insulin or diabetic pills to control blood sugar), race (white/black/other), age (five-year cohorts beginning with age thirty), and sex. Since BP is continuous, ordinary least squares (OLS) regression was used, with separate equations for systolic and diastolic BP, and for men and women.[9] Coefficients had the correct sign, with the expected clinically observed relationships: BP increased with age and BMI and was higher for blacks than for whites. The adjusted R^2 measure for the systolic equation (used later in risk equations) was approximately 0.2 (men) and 0.4 (women), within the range of other similar studies. Coefficients for black race, older age and BMI variables were significant at the .01 level.[10] Two risk factors—sodium

intake and exercise—could not be included in the predictive model because data were available only for 1999–2000.[11]

To predict BP in the absence of antihypertensive drug therapy, the estimated structural relationship based on data from 1959–62 was applied to observed values of the explanatory variables for people in the 1999–2000 NHANES sample. Following definitions by the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V), individuals were assigned to one of five categories based on their predicted and observed systolic (SBP) and diastolic (DBP) values: optimal, normal, high normal, Stage I hypertension, and Stage II hypertension.[12] As adopted by Peter Wilson and colleagues, where SBP and DBP categories differed, the more hypertensive was used. The resulting distribution of predicted BPs for 1999–2000 was compared with the distribution of observed BPs. After we controlled for changes in the identified risk factors for which data are available, the difference between the two distributions was attributed to antihypertensive therapy.

We note that the estimate is the result of a residual analysis. Factors that are not controlled for could affect BP trends, such as sodium intake and exercise. Sensitivity analysis of later NHANES data sets suggests that including these variables would not have a large effect on the estimated relationship. David Goff and colleagues and other researchers suggest a downward trend in cohort BP over time as a result of unknown, population-level factors, which would reduce the estimated impact of medication.[13] Even assuming a downward cohort effect equal to all of the observed improvement in the lowest-decile untreated BPs would reduce our estimates of benefits only modestly, from a 9 percent to an 8 percent reduction in premature deaths in 2001.[14]

■ **Estimating the impact of antihypertensive therapy on health outcomes.** We modeled the impact of BP on mortality and CVD events (stroke and MI). The impact of antihypertensive therapy on risk of death and total deaths from CHD was estimated using Framingham Heart Study risk equations estimated by Wilson and colleagues. These equations indicate how BP affects CHD mortality, controlling for other risk factors. Using population life tables and cause-of-death statistics from the National Center for Health Statistics (NCHS), we translated these changes in risk into changes in life expectancy.[15]

The impact of antihypertensive therapy on risk of stroke and MI was calculated using Framingham Heart Study risk equations estimated by Keaven Anderson and colleagues.[16] These risk ratios were combined with hospitalization data from the National Hospital Discharge Survey (NHDS) to estimate total hospitalizations avoided.

In each of these static calculations, we took the current population as given. Of course, without antihypertensive treatment, more people with hypertension would have died, and there would be fewer in the population today to experience strokes and MI. This has the effect of overstating our estimate of the impact in

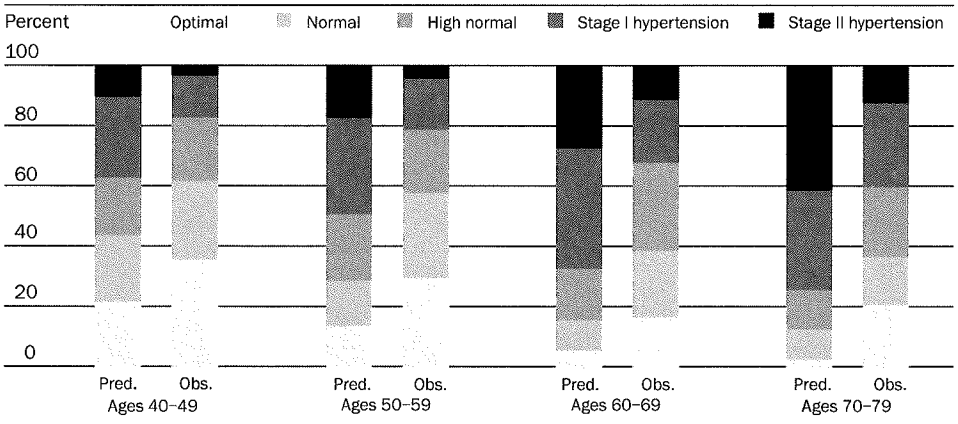
2001 but ignores any premature deaths prevented by antihypertensives prior to 2001. On the other hand, our calculation of avoided deaths, strokes, and MIs likely underestimates the impact of antihypertensive medication within each age-sex cohort because it ignores the curvilinear impact of blood pressure on the probability of death, stroke, and MI.[17] The two factors will affect our estimates in opposite directions. In the absence of a detailed simulation model of the interactive effects of changes in risk factors for each year over time, we assumed a static population and an average increase in the risk of death, stroke, and MI for each age-sex cohort.

Study Results

Exhibits 1 and 2 compare weighted average predicted and observed blood pressures for men and women (1999–2000). In the absence of antihypertensive drug therapy, average BPs for the population age forty and older would have been 10–13 percent higher (10.0 percent and 10.7 percent for men, 10.4 percent and 12.9 percent for women for SBP and DBP, respectively).

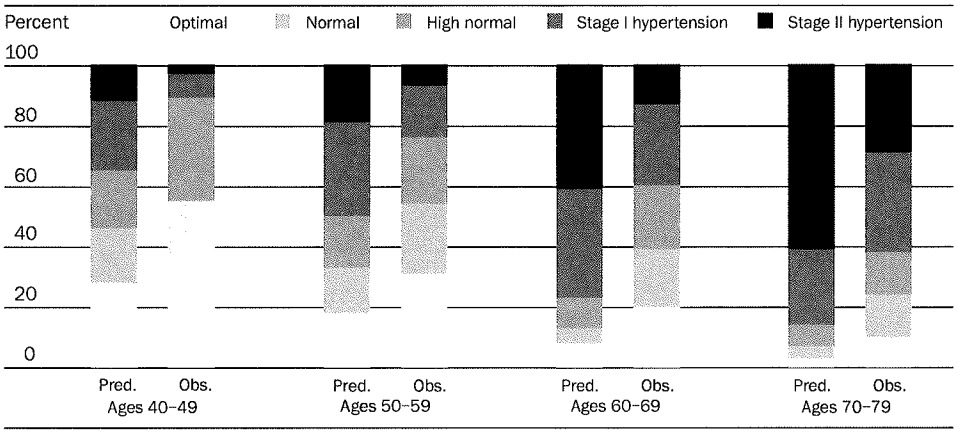
Women ages 70–79 exhibited the greatest difference between predicted and observed BPs, with 61 percent predicted and 29 percent observed with Stage II hypertension, compared with 41 percent and 12 percent, respectively, for men ages 70–79. However, these women also experienced rates of Stage II hypertension that were 2.5 times higher than those of their male peers. We calculated confidence intervals (CIs) on the percentages of men and women in each predicted blood pressure category using methods from the literature for simultaneous CIs on multinomial proportions (Exhibit 3).[18]

EXHIBIT 1
Blood Pressure Among Men, Predicted Without Drugs And Observed With Drugs, By Blood Pressure Level And Age Group, 1999–2000



SOURCE: Authors' calculations and comparison with 1999–2000 National Health and Nutrition Examination Survey (NHANES) data.
NOTES: Optimal: systolic blood pressure (SBP) <120, diastolic blood pressure (DBP) <80. Normal: SBP 120–129, DBP 80–84. High normal: SBP 130–139, DBP 85–89. Stage I hypertension: SBP 140–159, DBP 90–99. Stage II hypertension: SBP >/=160, DBP >/=100.

EXHIBIT 2
Blood Pressure Among Women, Predicted Without Drugs And Observed With Drugs, By Blood Pressure Level And Age Group, 1999–2000



SOURCE: Authors' calculations and comparison with 1999–2000 National Health and Nutrition Examination Survey (NHANES) data.
NOTES: Optimal: systolic blood pressure (SBP) <120, diastolic blood pressure (DBP) <80. Normal: SBP 120–129, DBP 80–84. High normal: SBP 130–139, DBP 85–89. Stage I hypertension: SBP 140–159, DBP 90–99. Stage II hypertension: SBP >/=160, DBP >/=100.

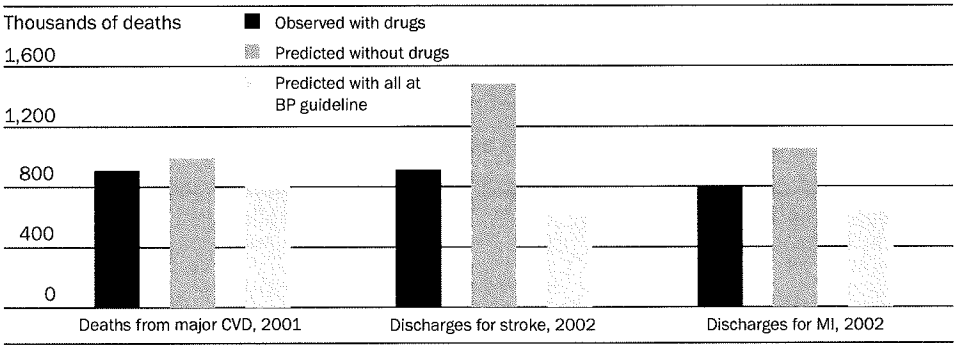
Exhibit 4 presents the predicted impact of better-controlled blood pressures on deaths from CVD (2001) and on hospital discharges for stroke and MI (2002) and the potential for further improvements if all achieved guideline blood pres-

EXHIBIT 3
Predicted Blood Pressures, By Sex And Age Cohort, 1999–2000

	Men, by age group (years)			
Blood pressure	**40–49**	**50–59**	**60–69**	**70–79**
Optimal	22% (16, 28)	14% (9, 21)	6% (3, 10)	3% (1, 7)
Normal	22 (17, 29)	15 (10, 22)	10 (7, 15)	10 (6, 16)
High normal	19 (14, 26)	22 (16, 30)	17 (12, 22)	13 (8, 20)
Stage I hypertension	27 (21, 33)	32 (25, 40)	40 (34, 47)	33 (26, 41)
Stage II hypertension	10 (7, 16)	17 (12, 24)	27 (21, 33)	41 (33, 50)
	Women, by age group (years)			
	40–49	**50–59**	**60–69**	**70–79**
Optimal	28% (22, 35)	18% (13, 25)	8% (5, 13)	3% (1, 8)
Normal	18 (13, 24)	15 (10, 21)	5 (3, 9)	4 (2, 9)
High normal	19 (14, 25)	17 (12, 24)	10 (7, 15)	7 (4, 13)
Stage I hypertension	23 (18, 30)	31 (25, 39)	36 (30, 44)	25 (19, 33)
Stage II hypertension	12 (8, 17)	18 (13, 25)	40 (34, 48)	61 (52, 69)

SOURCE: Authors' calculations, applying methods from W. L. May and W.D. Johnson, "A SAS Macro for Constructing Simultaneous Confidence Intervals for Multinomial Proportions," *Computer Methods and Programs in Biomedicine* 53, no. 3 (1997): 153–162.
NOTE: 95 percent confidence interval (CI) is in parentheses.

EXHIBIT 4
Deaths In 2001 And Hospital Discharges For Strokes And Myocardial Infarctions (MIs) In 2002 For Men And Women: Observed With Antihypertensive Drugs, Predicted Without Drugs, And Potential With All At Blood Pressure (BP) Guideline



SOURCE: Authors' calculations, applying estimated relative risk ratios to hospital discharge figures from the National Hospital Discharge Survey and cause-of-death figures from the National Center for Health Statistics.
NOTE: CVD is cardiovascular disease.

sures. Applying the change in risk of death to total deaths for each sex-age cohort, we estimated that 86,000 excess premature deaths from cardiovascular disease (50,000 men, 36,000 women) would have occurred in 2001 among the U.S. population age forty and older without antihypertensive drug therapy. Ninety-five percent CIs were calculated for the estimated relative risk ratios. When summed across each sex-age cohort, estimated avoided deaths ranged from 37,295 to 62,473 men, and from 25,876 to 46,553 women.[19] For adults age forty and older, observed 2001 total deaths and deaths from major CVD would be 4 percent and 9 percent lower, respectively, than predicted levels with untreated BPs. Because of potential competing risks, these estimates represent reductions in premature deaths due to CVD; reductions in total mortality from all causes in a given year might be lower.

To put these results in perspective, 86,000 deaths would have approached total deaths from accidents (98,000), the fifth leading cause of death in 1999–00, and would have exceeded all deaths from influenza and pneumonia (64,000), the seventh leading cause and a major cause of death in the elderly.[20]

We also considered what would happen if all people with hypertension took medication that was effective and did so with the right dosage and frequency. If all patients with Stage I or II hypertension who reported being untreated had been treated, as recommended in JNC 7, and if all treated patients achieved normal BPs, an additional 89,000 fewer premature deaths from major CVD would have occurred in 2001.[21] Hence, achieving effective blood pressure control would be approximately equivalent to eliminating all deaths from accidents, or from influenza and pneumonia combined. In addition, it would be roughly equivalent to the estimated number of people who die of medical errors annually.[22]

Translating these figures into increased life expectancy associated with antihypertensive drug therapy, and averaging the benefit over the entire popula-

tion, we estimated an increase of 0.5 years (men) and 0.4 years (women) if effective antihypertensive medication were widely used. Averaged over only the population with predicted Stage I or Stage II hypertension, we estimated improvements of 0.9 years (men) and 0.6 years (women).

■ **Impact of better-controlled blood pressure on MI and stroke.** In the absence of antihypertensive drug therapy, we estimated that there would have been 572,000 more hospital discharges for stroke in 2002 (162,000 men, 410,000 women) and 261,000 more discharges for MI (87,000 men, 174,000 women). Ninety-five percent CIs were calculated for the estimated relative risk ratios, resulting in estimated avoided hospital discharges for stroke that range from 479,646 to 664,214 (men) and 348,004 to 471,868 (women), and for MI that range from 204,296 to 317,106 (men) and 136,706 to 210,964 (women). Estimated hospital discharges avoided represent a 38 percent reduction in discharges for stroke and a 25 percent reduction for MI, compared to predictions with untreated BPs. Much of this improvement represents stroke and MI avoided altogether, rather than delayed. If all of those who avoided stroke and MI had highest risk (that is, average Stage II blood pressures) and had average remaining years of life (calculated by five-year age cohort) in which to experience another event, we calculated that they would have experienced only 7 percent of these strokes and 5 percent of these MIs later in life. We also calculated considerable improvements if blood pressure guidelines were achieved for all. If all untreated patients with Stage I or II hypertension had been treated and all achieved normal BPs, there would have been 278,000 (stroke) and 142,000 (MI) fewer hospital discharges in 2002 than actually occurred.

These results are generally consistent with cohort study findings of substantial mortality, stroke, and MI benefits from lower BP and other risk factors, and with randomized clinical trials showing reductions to BP goal from individual and combination antihypertensive treatments.[23]

■ **Benefit-to-cost ratio of antihypertensive therapy.** To value these improvements in dollars, we followed the literature and assumed that each year of additional life in good health is worth approximately $90,000, or $100,000 a year, less $10,000 in support costs.[24] The benefits of roughly one-half year of longer life, discounted over an average lifespan at a 3 percent annual rate, are $5,117 (men) and $3,454 (women) per person. In comparison, lifetime spending on antihypertensive drugs across the treated and untreated population averages $520 (men) and $539 (women), also discounted over an average lifespan at a 3 percent annual rate.[25] Since long-term support costs have been subtracted from benefits, this figure represents the additional costs associated with medication. Although we did not subtract unknown costs resulting from potential side effects, we concluded that benefits are greater than costs. We calculated an approximate benefit-to-cost ratio of 10:1 for men and 6:1 for women.

Previous studies have concluded that antihypertensive treatment is likely cost-effective compared with other possible investments; Milton Weinstein reports es-

timates of the number of quality-adjusted life-years (QALYs) achieved with each $1 million spent on antihypertensive drug therapy as between 20 and 50 QALYs (antihypertensive treatment, DBP 95–104) to more than 200 QALYs (beta-blockade post-MI, high risk). As a benchmark, $1 million spent for dialysis for end-stage renal disease is estimated to yield ten to twenty QALYs.[26] Our findings show that these favorable results can be obtained in actual practice.

Reduced hospitalizations for stroke and MI would increase calculated net benefits even further. Using data from the literature for average hospital costs for CHD and cerebrovascular disease and assuming that hospital costs represent 70 percent of direct medical costs in the year following stroke and MI, we estimated 2002 total direct medical costs avoided as a result of fewer strokes and MI of $10.7 billion and $5.8 billion, respectively (Exhibit 5).[27] In comparison, personal health care spending on antihypertensive prescription drugs totaled an estimated $8.8 billion in 1998.[28] Including the impact of antihypertensive drugs on the quality of life and work productivity would increase the benefit-to-cost ratio still further.

Summary And Policy Implications

By many measures, hypertension is much better treated now than in the past. Although further efforts are still needed to bring health benefits to all, awareness, treatment, and control of hypertension have shown considerable improvement in

EXHIBIT 5
Estimated Avoided Direct Costs Resulting From Improved Blood Pressures, 2002

	Coronary heart disease	Cerebrovascular disease
Total direct expenditures (millions $, 2002)[a]	$58,470	$29,786
Hospital care	33,352	12,358
All other	25,117	17,428
Avoided hospital discharges due to BP improvement (thousands, 2002)[b]	261	572
Average hospital care expenditures per discharge ($, 2002)[c]	$15,628	$13,063
Avoided direct expenditures (millions $, 2002)[d]	$ 5,845	$10,719
Hospital care	4,092	7,503
All other	1,754	3,216

SOURCES: See below.

NOTES: Estimated avoided hospital discharges for coronary heart disease include myocardial infarction (MI) only.

[a] Authors' estimates, applying approach from T.A. Hodgson and A.J. Cohen, "Medical Care Expenditures for Selected Circulatory Diseases: Opportunities for Reducing National Health Expenditures," *Medical Care* 37, no. 10 (1999): 994–1012, updated with 2002 data from Centers for Medicare and Medicaid Services, "National Health Expenditure Amounts, and Annual Percent Change by Type of Expenditure: Selected Calendar Years 1999–2015," http://www.cms.hhs.gov/NationalHealthExpendData/downloads/proj2005.pdf (accessed 5 October 2006).

[b] Authors' estimates from statistical model.

[c] Calculated by dividing total direct expenditures (hospital care) by hospital discharge total from American Heart Association, "Heart Disease and Stroke Statistics—2005 Update" (Dallas: AHA, 2005).

[d] Assumes that hospital care expenditures represent 70 percent of direct medical costs, per T.N. Taylor et al., "Lifetime Cost of Stroke in the United States," *Stroke* 27, no. 9 (1996): 1459–1466.

"Private insurance plans are unlikely to bear the future medical costs of the underuse of effective medicines today."

the past few decades.[29] The estimated impact of antihypertensive therapy on BP is substantial: approximately 10 percent (SBP) and 13 percent (DBP) lower blood pressure for both men and women age forty and older, compared with predicted untreated BP. Better-controlled BP translated into 9 percent fewer deaths from major CVD in 2001 and 38 percent and 25 percent fewer hospital discharges for stroke and MI in 2002, respectively, compared with predicted levels in the absence of drug therapy. In comparison to these approximately 86,000 avoided deaths, U.S. mortality from motor vehicle accidents totaled approximately 42,000 in 2001.[30]

Although the benefits of antihypertensive therapy have been substantial, major opportunities remain to extend drug treatment to more who could benefit. We estimated that life expectancy could increase an additional 0.3 years (men) and 0.1 years (women) if therapy were extended to all with Stage I or Stage II hypertension not currently treated with medication, and a further 0.2 years for both men and women if those treated achieved normal BP. These figures translate into an additional 89,000 avoided premature deaths from major CVD and an additional 278,000 (stroke) and 142,000 (MI) avoided hospital discharges, compared with actual 2002 levels. We have achieved approximately half of the possible health gains.

These results have several important implications. The first is for the value of increased medication costs. Our estimates suggest that antihypertensive medication has a benefit-to-cost ratio of 6:1 (women) to 10:1 (men), both of which are highly cost-effective. With an aging population, the total burden of CVD on individuals, their families, and society overall will increase. As one of the most major modifiable health risks and in light of the highly attractive benefit-to-cost ratio we calculated, hypertension control should receive top priority for outreach, education, and compliance efforts.

■ **Medicare.** One of the central questions for policymakers is why we don't do better in controlling hypertension if the societal return on investment is so high. Underuse of effective, cost-efficient therapy continues to be a major public health challenge; the case of antihypertensive therapy is one major example. This is particularly important in the context of the recent implementation of the Medicare Part D prescription drug benefit and its potential for improving the health of elderly and disabled Americans. One issue is a lack of insurance coverage. Uninsured people are less likely than their insured peers are to be screened and diagnosed for hypertension and to comply with recommended pharmaceutical therapy. They are correspondingly more likely to experience potentially fatal acute cardiovascular episodes.[31]

Even for the insured, however, the current system provides too few incentives to correct underuse. Private insurance plans are unlikely to bear the future medi-

cal costs of the underuse of effective medicines today, since members will move to other plans or reach Medicare eligibility before many of the adverse events occur. With the new Part D drug benefit, Medicare will have an unprecedented opportunity to align incentives in prevention and acute treatment, particularly for members of Medicare Advantage (MA) plans that include both drug and medical benefits. Thus far, Medicare has not taken advantage of that opportunity to any great extent. Two ideas are particularly promising to address this issue. First, plans could reduce patient cost sharing on drugs for which there is a strong body of evidence documenting best practice and cost-saving treatment. The literature suggests that ACE inhibitors for diabetics are one such example.[32] Our findings suggest that antihypertensive medication could be another. For these medications, cost sharing might be eliminated entirely, to eliminate disincentives to take efficacious and cost-effective medication.

Second, Medicare could experiment with pay-for-performance (P4P) approaches that reward physicians for improved BP control. Physician reimbursement could be structured to reward bringing untreated hypertensive patients into treatment and maintaining patients at target BPs. Each of these could be highly cost-effective investments.

■ **Evaluating medical costs.** Our results also have implications for overall evaluation of medical costs. Earlier research largely focused on assessing whether or not care for acute conditions was "worth it." This examination of one of the most widespread chronic diseases in the United States—and increasingly the developed world—suggests that spending on pharmaceutical interventions for chronic diseases might likewise have resulted in benefits far exceeding their costs. Further research is needed to confirm whether similar results would be associated with other major chronic diseases, such as congestive heart failure, diabetes, asthma, or different cancers.

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NOTES

1. D.M. Cutler and M. McClellan, "Is Technological Change in Medicine Worth It?" *Health Affairs* 20, no. 5 (2001): 11–29.
2. See, for instance, ibid.; D.M. Cutler and E. Meara, "The Technology of Birth: Is It Worth It?" in *Frontiers in Health Policy Research*, vol. 3, ed. A. Garber (Cambridge, Mass.: MIT Press, 2000), 33–67; E.R. Berndt et al., "The Medical Treatment of Depression, 1991–1996: Productive Inefficiency, Expected Outcome Variations, and Price Indexes," *Journal of Health Economics* 21, no. 3 (2002): 373–396; I. Shapiro, M.D. Shapiro, and D.W. Wilcox, "Measuring the Value of Cataract Surgery," in *Medical Care Output and Productivity*, ed. D.M. Cutler and E.R. Berndt (Chicago: University of Chicago Press, 2001); and D.M. Cutler and M. McClellan, "The Productivity of Cancer Care" (Unpublished paper, Harvard University, 2001).
3. Authors' calculations from 1999–2000 National Health and Nutrition Examination Survey (NHANES) data.
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9. To allow for nonlinearities, an alternative specification was tested with the continuous BMI variables in the BP equation replaced by six categories from the literature: "less than or within normal BMI range," "marginally overweight," "overweight," "very overweight," "severely obese," and "morbidly/super obese," from K. Renquist, "Obesity Classification," *Obesity Surgery* 7, no. 6 (1997): 523. The relationship between BP and BMI was found to be linear for women and weakly concave for men.
10. More detail can be found in an online Technical Appendix, at http://content.healthaffairs.org/cgi/content/full/26/1/97/DC1.
11. A sensitivity analysis of the impact of the sodium intake and exercise variables on BP, using 1999–2000 data for untreated individuals, was conducted, with the conclusion that neither increased the explanatory power of the model significantly. Predicted BP distributions were nearly identical with or without these variables, as were estimated BMI and BMI^2 coefficients, with the R^2 measure increasing only at the third decimal point. Results were essentially unaffected when the dependent variable was log-transformed.
12. "The Fifth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V)," *Archives of Internal Medicine* 153, no. 2 (1993): 154–183. JNC V BP categories were used in the risk equations of Peter Wilson and colleagues; see Note 15.
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14. Details are available in the online Technical Appendix; see Note 10.
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17. The risks of death from cardiovascular disease, stroke, and MI increase more than proportionally with BP. Therefore, for any sex-age cohort, risk is higher for people with higher BP. In estimating avoided deaths resulting from better-controlled BP, we calculated relative risks for each sample observation and averaged

them for the total sex-age cohort according to their sample weights. This average relative risk is multiplied by the observed number of deaths for that cohort and the number of avoided deaths calculated. But it is likely that those with CVD have higher BPs than others in their sex-age cohort. If so, deaths would increase by more than the average relative risk, and we would have underestimated the number of avoided deaths resulting from better-controlled BP. The same logic applies to avoided strokes and MI.

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